

Characterization of Aeroneb vibrating mesh nebulizers and implications for ALICE-Cloud technology

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Vibrating mesh nebulizers are becoming increasingly more prevalent in toxicological, pharmaceutical and clinical settings. Their high aerosol mass output rates (up to 1 ml/min) at droplet size distributions relevant for pulmonary drug delivery combined with air-less operation (no air flow required) makes them ideal for many applications. In spite of their wide-spread use there is a lack of performance characterization for vibrating mesh nebulizers. In this study the performance of sixteen Aeroneb vibrating mesh nebulizers (Aerogen Inc.) has been characterized and the impact of varying Aeroneb performance parameters on the ALICE-Cloud technology (Lenz et al., 2014) for aerosolized delivery of liquid substances to air-liquid interface cell cultures has been investigated.

The investigated sixteen Aeroneb nebulizers belong to three different models: Aeroneb Pro (n=12), Lab Standard (1) and Lab Small (3). Phosphate buffered saline (PBS) is nebulized with each of the investigated nebulizers and the aerosol mass output rate was determined by measurement of the required time for nebulization of a known amount of liquid. The particle number size distribution is measured with a single particle light scattering spectrometer (INAS, Palas) using ionic liquid droplets produced by nebulization and subsequent drying of 1:50 ionic liquid (IL-0007-IoLiTec). The number size distribution of the droplets was converted into volume size distribution assuming spherical droplet shape. Droplet size was also characterized by laser diffraction (HELOS, Sympatec), one of the standard sizing techniques for medical nebulizers. The speed of the aerosol cloud emitted by the nebulizers is measured for the first time with a specifically designed optically triggered stop watch consisting of two light gates separated by a known distance.

The nebulizer output rates varied between 0.30 and 0.80 ml/min. For ten of the sixteen nebulizers the volume median diameter (VMD) of the droplet size distribution varied between 3.7 and 6.8 μm (Figure 1). There was good agreement (within 15%, $R^2 = 0.95$) between the VMD determined by single particle light scattering and laser diffraction (Figure 1). The VMD of one of the investigated Aeroneb nebulizers was outside the manufacturer specified range (5.1 μm instead of 4.0 μm for Aeroneb Lab Small). There was only a weak correlation between aerosol output rate and VMD ($R^2 = 0.27$). The speed of the emitted aerosol cloud was about 4.0 m/s, independent of Aeroneb model. Only one of the

investigated nebulizers had a somewhat higher cloud speed of 5.0 m/s.

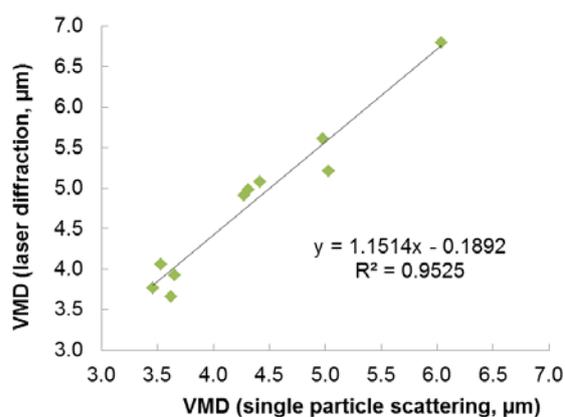


Figure 1. Scatter plot of volume median diameter (VMD) of droplet size distribution measured by laser diffraction or by single particle light scattering.

Finally, the impact of the nebulizer characteristics on the performance of the ALICE-CLOUD technology (VITROCELL-CLOUD 12/9, VITROCELL Systems) for dose-controlled aerosol-cell delivery was investigated. Only the aerosol output rate showed a statistically significant effect resulting in moderately reduced ALICE-Cloud performance with respect to aerosol-cell delivery efficiency and uniformity of aerosol deposition for nebulizer output rates above 0.45 ml/min.

In summary, the manufacturer specifications for the aerosol output rate and droplet size of Aeroneb vibrating mesh nebulizers could be confirmed. For the first time, the speed of the emitted aerosol cloud was determined and found to be 4.0 -5.0 m/s. Moreover, the observed inter-device variability of Aeroneb output has a moderate effect on aerosol-cell delivery characteristics of the ALICE-Cloud technology.

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